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Clinical and Angiographic Correlates and Outcomes of Suboptimal Coronary Flow in Patients With Acute Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention

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OBJECTIVES The purpose of this study was to determine the clinical and angiographic correlates and outcomes of patients with suboptimal coronary flow after primary percutaneous coronary interventions (PCI).

BACKGROUND The clinical and angiographic correlates and outcomes of Thrombolysis in Myocardial Infarction (TIMI) ≤2 flow in patients treated with primary PCI are not known.

METHODS We evaluated 3,362 patients with ST elevation myocardial infarction enrolled in various Primary Angioplasty in Myocardial Infarction trials, who underwent primary PCI.

RESULTS Post-procedural final TIMI ≤2 flow occurred in 232 (6.9%) patients. Multivariate analysis identified age ≥70 years (odds ratio [OR], 1.6; 95% confidence interval [CI], 1.1 to 2.2), diabetes (OR 1.9; 95% CI, 1.3 to 2.7), symptom onset to emergency room presentation (OR 1.1; 95% CI, 1.1 to 1.2); initial TIMI ≤1 flow (OR 3.2; 95% CI, 1.9 to 5.5), and left ventricular ejection fraction <50% (OR 1.7; 95% CI, 1.2 to 2.4) as independent correlates of final TIMI ≤2 flow. In-hospital (composite of reinfarction, ischemic target vessel revascularization, or death, as well as these events individually) and one-year (reinfarction and/or death) events occurred more frequently in patients with TIMI ≤2 flow. The Cox proportional hazards model identified TIMI ≤2 flow to be independently associated with one-year mortality (hazard ratio 3.8, 95% CI, 2.5 to 5.7).

CONCLUSIONS Final TIMI ≤2 flow, although uncommon after primary PCI, was strongly associated with hospital and one-year adverse events. The clustering of final TIMI ≤2 flow in high-risk groups may partially explain the poor prognosis of these patients. Awareness of these risk factors may be useful to clinicians to triage and treat patients undergoing primary PCI. (J Am Coll Cardiol 2003;42:1739–46) © 2003 by the American College of Cardiology Foundation

Reperfusion therapy is the cornerstone of the treatment of patients with acute ST elevation myocardial infarction (STEMI) (1). Many randomized clinical trials have shown that primary percutaneous coronary intervention (PCI) is superior to thrombolytic therapy in the treatment of patients with STEMI (2–5). Nevertheless, the occurrence of Thrombolysis in Myocardial Infarction (TIMI) ≤2 flow remains the "Achilles heel" of primary PCI occurring in 2% to 37% of patients (2–13), even in the era of the routine use of stents and newer antithrombotic and antiplatelet agents, strategies shown to improve the outcomes of patients undergoing primary PCI (14–16). Furthermore, TIMI ≤2 flow has been shown to be associated with increased incidence of major in-hospital adverse events in these patients (10–12). Despite this, the clinical correlates of TIMI ≤2 flow in patients undergoing primary PCI have not been well characterized. Additionally, the in-hospital and long-term outcomes have not been studied in a large group of patients undergoing primary PCI. The purpose of our study was to objectively characterize contemporary clinical and angiographic variables associated with the risk of TIMI ≤2 flow and the in-hospital and long-term outcomes associated with it in a large cohort of patients undergoing primary PCI.

METHODS

Patient population. The Primary Angioplasty in Myocardial Infarction (PAMI) studies prospectively enrolled patients with STEMI into seven clinical trials (PAMI-1, PAMI-2, PAMI Stent Pilot, Stent PAMI, Local PAMI, Air PAMI, and PAMI–No Surgery on Site) (2,6,17–23). Two of these trials (6,18) also enrolled patients into concomitant registries. The rationale, methodology, and the results of the individual PAMI studies have been previously published (2,6,17–23). Patients were included in these investigations if they were ≥18 years of age with STEMI presenting within 12 h of their symptom onset. Acute

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Abbreviations and Acronyms

CI = confidence interval
LVEF = left ventricular ejection fraction
MACE = major adverse cardiovascular events
OR = odds ratio
PAMI = Primary Angioplasty in Myocardial Infarction
PCI = percutaneous coronary intervention
STEMI = ST elevation myocardial infarction
TIMI = Thrombolysis In Myocardial Infarction

STEMI was defined by the following criteria: ST elevation of at least 1 mm in ≥2 contiguous leads or presumed new left bundle-branch block on the presenting 12-lead electrocardiogram. Patients were excluded from these trials if they had contraindications to reperfusion (2), had received thrombolytic therapy for index STEMI, had renal failure, cardiogenic shock, or life expectancy less than one year; also excluded were those with child-bearing potential (unless the result of a recent pregnancy test was negative), or those with known contraindications to aspirin, heparin, or ticlopidine in later PAMI trials (6,19–23). Furthermore, patients randomized to the thrombolytic arm (PAMI-1 and Air-PAMI) or those in whom primary PCI was not attempted (defined as no attempt to pass a guide wire) were also excluded from this analysis. Informed consent was obtained from all patients by the study investigators or coordinators at the respective institutions. For the purpose of this study, we pooled the clinical, demographic, angiographic, and in-hospital clinical events and outcomes data on 3,362 patients enrolled in these trials who underwent primary PCI.

Data collection and angiographic analyses. Research nurses or a coordinator at each site collected data prospectively on prespecified data elements on a case report form in all trials. These data included baseline demographics, medical history, medications, procedures, complications, and clinical events. Follow-up was obtained at one year by means of self-administered questionnaire, by telephone interview or follow-up visit to the physician. Completed case report forms were sent to the PAMI coordinating site at Beaumont Hospital, Royal Oak, Michigan, where the data were entered into an Access data base. Independent data monitoring was performed through onsite visit of the participating sites to verify records of all patients. The cineangiograms obtained at the time of index intervention were analyzed at the core laboratory site, which assessed coronary anatomy, TIMI flow grades, percent diameter stenosis, left ventricular ejection fraction (LVEF), and angiographic outcomes of the intervention.

Definitions, comparison groups, and study end points. Suboptimal coronary flow was defined as final TIMI ≤2 flow and normal flow as TIMI 3 flow in the infarct-related artery. Reinfarction was defined as recurrent clinical symptoms or development of new electrocardiographic changes accompanied by new elevation of creatine kinase and creatine kinase MB enzyme levels. Ischemia-driven target vessel revascularization was defined as PCI or coronary artery bypass surgery of the index infarct-related artery prompted by symptoms or objective evidence of ischemia. Sustained hypotension was defined as systolic blood pressure <80 mm Hg unresponsive to intravenous fluids, requiring vasopressors for >1 h or intraaortic balloon pump. For this study, we compared the baseline clinical, demographic, angiographic, and in-hospital adverse events of patients with a final TIMI ≤2 (suboptimal flow) and those with TIMI 3 flow (normal flow). The principal outcomes of interest for the current study included the differences in the hospital and one-year mortality, and hospital and one-year incidence of major adverse cardiovascular events (MACE, defined as death, or reinfarction, or ischemia-driven target vessel revascularization) between the two comparison groups.

Statistical analysis. Summary statistics are presented as frequencies and percentages or as medians as appropriate. Comparisons between groups (TIMI ≤2 vs. TIMI 3 flow) were made using the two-tailed Wilcoxon rank sum test for continuous variables and the chi-square or Fisher exact test (when expected frequency count in the cell <5) for categorical variables as appropriate. In all cases, missing data were not defaulted to negative and denominators reflect cases reported. Stepdown multivariable logistic regression was constructed to identify clinical predictors of TIMI ≤2 flow using variables showing marginal association with it on univariate testing ($p < 0.10$). Variables were reviewed for clinical significance before testing. Variables included in the first step of the model development included age ≥70 years, gender, time of symptom onset to arrival in the emergency room, medical history (diabetes, hypertension, previous coronary artery bypass surgery, and smoking), presenting features (pulse >100 beats/min, systolic blood pressure <100 mm Hg, and Killip class >1), concomitant treatments (stents), and angiographic findings (left anterior descending as infarct-related artery [vs. other coronary arteries], initial TIMI flow, and percent stenosis of the infarct-related artery and LVEF <50%). Only variables with a significant ($p < 0.05$) association with TIMI ≤2 flow were included in the final regression models. Adjusted odds ratios and accompanying 95% confidence intervals (CIs) were computed to determine the effect of each variable in the final model on the risk of TIMI ≤2 flow. Diagnostic routines (the Hosmer-Lemeshow test for lack of fit and likelihood ratio test) were used for the final model selection. The c-statistic was calculated to evaluate model discrimination. Finally, to determine the impact of TIMI ≤2 flow on one-year mortality, we used the Cox proportional hazards model to adjust for baseline differences in clinical characteristics between the two groups. Hazard ratio and 95% CI were constructed to provide estimate of risk posed by TIMI ≤2 flow on long-term (one-year) mortality. SAS software (version 8.0, SAS Institute, Cary, North Carolina) was used for all analyses.

Table 1. Baseline Characteristics of Study Patients

	TIMI Flow = 3 (n = 3,130)	TIMI Flow ≤2 (n = 232)	
	n (%)		p Value
Mean age (SD), yrs	61 (12)	65 (12)	< 0.0001
Age ≥70 yrs	806 (26.0)	84 (36.0)	0.0005
Females	828 (26.0)	63 (27.0)	0.82
Mean BMI (SD), [median], kg/m^2	27.6 (4.8) [26.8]	27.0 (4.5) [26.6]	0.18
Onset of symptom to ER, mean (SD) [median], min	152 (144) [105]	201 (237) [120]	0.0082
Onset of symptom to balloon, mean (SD) [median], min	283 (176) [230]	317 (194) [250]	0.0059
ER to balloon, mean (SD) [median], min	143 (161) [113]	145 (119) [120]	0.27
Past medical history			
Angina	381 (17.0)	29 (16.0)	0.62
Myocardial infarction	431 (14.0)	35 (15.0)	0.59
Congestive heart failure	67 (2.2)	7 (3.1)	0.37
Diabetes	482 (15.0)	56 (24.0)	0.0005
Hypertension	1,395 (45.0)	118 (52.0)	0.046
Stroke or transient ischemic attack	155 (5.0)	17 (7.5)	0.099
Hyperlipidemia	913 (40.0)	62 (36.0)	0.33
Peripheral vascular disease	178 (5.8)	16 (7.3)	0.38
Current tobacco smoking	1,310 (42.0)	82 (36.0)	0.070
Ever smoked	1,968 (66.0)	132 (59.0)	0.032
PCI	302 (9.7)	16 (7.0)	0.17
CABG	111 (3.9)	15 (6.9)	0.033
Family history of CAD	829 (36.0)	62 (34.0)	0.63
Presentation			
Pulse mean (SD), beats/min	87 (21)	92 (20)	0.0009
Pulse >100 beats/min	588 (21.0)	64 (29.0)	0.0035
Systolic blood pressure, mean (SD), mm Hg	111 (26)	108 (26)	0.032
Systolic blood pressure <100 mm Hg	860 (31.0)	82 (38.0)	0.047
Killip class >1	400 (12.9)	39 (17.3)	0.059
Medications before or during PCI			
Aspirin	2,323 (94.0)	177 (97.0)	0.12
Ticlopidine	1,126 (77.0)	100 (80.0)	0.45
Beta-blockers	878 (40.0)	66 (39.0)	0.69

BMI = body mass index; CABG = coronary artery bypass grafting; CAD = coronary artery disease; ER = emergency room; PCI = percutaneous coronary intervention; TIMI = Thrombolysis In Myocardial Infarction.

RESULTS

Clinical and angiographic characteristics of patients with and without final TIMI ≤2 flow (Tables 1 and 2). Of the 3,362 patients with STEMI undergoing primary PCI in the study, 232 (6.9%) had TIMI ≤2 flow after primary PCI. The number of patients with TIMI 0, 1, and 2 flows were 45 patients (1.3%), 25 patients (0.7%), and 162 patients (4.8%), respectively. Compared with the cohort with TIMI 3 flow, those with TIMI ≤2 flow were more likely to be 70 years or older, diabetic, hypertensive, with a history of previous coronary artery bypass surgery, but less likely to have ever smoked. There was a significant delay in the time to presentation to the emergency room after symptom onset in the group with TIMI ≤2 flow. Similarly, presentation with adverse hemodynamics such as heart rate >100 beats/min, blood pressure <100 mm Hg, and Killip class >1 was more common in patients with TIMI ≤2 flow.

Angiographic characteristics also differed between the two groups. Thus, patients with TIMI ≤2 flow were more likely to have initial TIMI flow ≤1, higher initial percent stenosis of infarct artery, left anterior descending as infarct-related artery, and LVEF <50%. The post-procedural final percent stenosis, presence of thrombus, and dissection of the infarct artery were also higher in patients with TIMI ≤2 final flow. Intracoronary arteriolar vasodilators (nitroprusside, nitroglycerin, verapamil, adenosine) were used in all patients with transient or final TIMI ≤2 flow. Glycoprotein IIb/IIIa receptor antagonist and intracoronary thrombolysis were used more frequently in patients with TIMI ≤2 flow. In contrast, intracoronary stents were used less frequently in patients with TIMI ≤2 flow.

Complications in catheterization laboratory, in-hospital and at one-year follow-up in patients with and without final TIMI ≤2 flow (Tables 2 and 3). Patients with TIMI ≤2 were more likely to have experienced an adverse event during the procedure. Thus, the incidence of sustained hypotension, requirement for endotracheal intubation or cardio-pulmonary resuscitation, and death was more common in this group of patients during primary PCI. These increased complications in the catheterization laboratory were further reflected in the higher rates of virtually all adverse events seen during hospital stay in patients with TIMI ≤2 flow, resulting in longer length of stay in these patients (Table 3).

JACC Vol. 42, No. 10, 2003
November 19, 2003:1739–46

Table 2. Angiographic Data and Cath-Lab Complications of Study Patients

	TIMI Flow = 3 (n = 3,130)	TIMI Flow ≤2 (n = 232)	
	n (%)		p Value
Angiographic data—initial			
Infarct-related artery			
Left main	19 (0.6)	3 (1.3)	
Left anterior descending	1,255 (40.7)	106 (46.9)	0.065
Left circumflex	444 (14.4)	26 (11.5)	0.23
Right coronary	1,341 (43.4)	86 (38.1)	0.11
Saphenous vein graft	28 (0.9)	5 (2.2)	
Initial TIMI flow grade			< 0.0001
0	1,996 (64.0)	182 (78.5)	
1	341 (10.9)	27 (11.6)	
2	496 (15.9)	22 (9.5)	
3	286 (9.2)	1 (0.4)	
Initial patency (TIMI flow 2 or 3)	782 (25.0)	23 (10.0)	< 0.0001
Initial percent stenosis, mean (SD) [median]	98 (5) [100]	99 (7) [100]	< 0.0001
LVEF, mean (SD)	49 (12)	45 (12)	< 0.0001
LVEF <50%	1,303 (48.0)	118 (64.0)	< 0.0001
Medications, intra-aortic balloon pump and stent use during the procedure			
Glycoprotein IIb/IIIa inhibitors	269 (9.6)	25 (14.9)	0.025
Thrombolytics	139 (5.1)	23 (15.5)	< 0.0001
Stents	1,174 (38.0)	69 (30.0)	0.018
Intra-aortic balloon pump	32 (7.0)	3 (13)	0.23
Initial activated clotting time, mean (SD)	246 (161)	260 (197)	0.78
Angiographic data post procedure			
Post-procedure percent stenosis, mean (SD) [median]	13 (13) [10]	40 (37) [30]	< 0.0001
Final stenosis >50%	12 (0.4)	62 (28%)	< 0.0001
Final thrombus	231 (8.5)	63 (39.9)	< 0.0001
Final dissection	415 (15.0)	41 (26)	0.0004
Cath-lab complications	396 (22.0)	43 (40.0)	< 0.0001
Bradyarrhythmias	297 (25.0)	26 (31.0)	0.19
Ventricular arrhythmias	130 (12.0)	6 (8.0)	0.27
Cardiopulmonary resuscitation	15 (0.8)	6 (4.8)	0.0012
Endotracheal intubation	14 (0.7)	7 (5.6)	< 0.0001
Hypotension	132 (7.5)	22 (19.0)	< 0.0001
Death	2 (0.1)	2 (1.7)	0.02

Cath-lab = cardiac catheterization laboratory; LVEF = left ventricular ejection fraction; TIMI = Thrombolysis In Myocardial Infarction.

The primary outcomes of interest for the PAMI studies, that is, in-hospital and one-year MACE, occurred more frequently in patients with TIMI ≤2 flow. The occurrence of death and reinfarction were also significantly higher in TIMI ≤2 flow during hospitalization and at one-year follow-up. The Cox proportional hazards model identified TIMI ≤2 flow as an independent predictor of one-year mortality (hazard ratio 3.8, 95% CI 2.5 to 5.6, $p < 0.0001$) (Fig. 1). In-hospital mortality and one-year mortality and MACE increased in patients with decreasing grades of TIMI flow (p for trend <0.0001 for all three outcomes, Fig. 2).

Clinical factors related to TIMI ≤2 flow (Table 4). Stepdown logistic regression analysis identified age ≥70 years, diabetes, time of symptom onset to emergency room arrival, initial TIMI ≤1 flow, and LVEF <50% as independent correlates of TIMI ≤2 flow (Table 4). The area under the receiver-operating curve for the model was 0.68. The Hosmer-Lemeshow statistic was not significant, indicating little deviation from perfect fit (chi-square 11.4, degrees of freedom 8, $p = 0.18$).

DISCUSSION

Findings of the present study. Failure to achieve normal flow is increasingly recognized as primary PCI is becoming a widely popular mode of reperfusion for patients with STEMI at many centers. The emergence of contrast echocardiography has allowed physicians to focus not only on epicardial coronary flow but also on microvascular perfusion (11). Our investigation provides a valuable insight into the incidence, clinical correlates, risk factors, and in-hospital and one-year outcomes of final TIMI ≤2 flow in a large cohort of STEMI patients undergoing primary PCI. The incidence of TIMI ≤2 flow is not insignificant, occurring in 1 of 14 patients undergoing primary PCI. Although the incidence of TIMI ≤2 flow in our study is lower than that observed in studies that used contrast echocardiography

Table 3. In-Hospital Complications and Long-Term Outcomes

	TIMI Flow = 3 (n = 3,130)	TIMI Flow ≤2 (n = 232)	
	n (%)		p Value
In-hospital complications			
Bradyarrhythmias	87 (2.8)	17 (7.3)	0.0001
Ventricular arrhythmias	117 (3.7)	14 (6.0)	0.081
Pulmonary edema	125 (4.5)	21 (13.0)	< 0.0001
Sustained hypotension	139 (5.3)	29 (18.0)	< 0.0001
Cardiopulmonary resuscitation	26 (0.9)	10 (4.5)	< 0.0001
Intraaortic balloon pump	50 (3.6)	13 (19)	< 0.0001
Ventricular septal rupture or severe mitral regurgitation	1 (0.03)	4 (1.7)	< 0.0001
Gastrointestinal bleeding	66 (2.6)	12 (6.5)	0.0028
Need for dialysis	11 (0.4)	2 (1.4)	0.15
Length of stay, mean (SD), days	6.4 (5.5)	8.1 (6.6)	< 0.0001
In-hospital outcomes			
Reinfarction	53 (1.7)	8 (3.5)	0.068
Ischemic TVR	96 (3.2)	10 (4.5)	0.31
Death	65 (2.1)	34 (15.0)	< 0.0001
MACE	175 (5.6)	47 (20.0)	< 0.0001
Disabling stroke	8 (0.3)	1 (0.4)	0.48
MACE or disabling stroke	181 (6.1)	47 (21.0)	< 0.0001
One-year outcomes			
Reinfarction	111 (4.4)	17 (9.3)	0.0028
Ischemic TVR	352 (15.0)	23 (13.0)	0.65
Death	133 (5.1)	47 (23.0)	< 0.0001
MACE	538 (20.0)	78 (37.0)	< 0.0001
Disabling stroke	16 (1.0)	2 (1.5)	0.64
MACE or disabling stroke	549 (30.0)	79 (47.0)	< 0.0001

MACE = major adverse cardiovascular events (reinfarction or ischemia-driven TVR or death); TIMI = Thrombolysis In Myocardial Infarction; TVR = target vessel revascularization.

along with coronary angiography (10,11), it compares favorably with that seen in most large-scale trials comparing the efficacy of primary PCI with thrombolysis or those comparing primary angioplasty with primary stenting (2–9,15–23). Furthermore, we found that the occurrence of TIMI ≤2 flow is not a benign event: it is associated with increased risk of complications not only in the cardiac catheterization laboratory and in-hospital but also at long-term follow-up. In contrast to patients treated with thrombolytic therapy, where rescue angioplasty in selected patients who fail thrombolysis may have a potential to improve outcomes, there are no good proven strategies to improve final TIMI ≤2 flow after primary PCI. As a result, the mortality in patients with TIMI 0, 1, and 2 flow in acute myocardial infarction patients treated with primary PCI patients is significantly greater than that observed in patients with similar grades of TIMI flow after thrombolysis (24). Not surprisingly, because of the higher complications in patients with TIMI ≤2 flow, the length of stay and resource utilization are also increased in these groups of patients. Thus, our findings underscore the importance of preventing the development of TIMI ≤2 flow as the optimal strategy to improve outcomes and decrease resource utilization in patients undergoing primary PCI, as once no-reflow occurs the outcomes are relatively dismal.

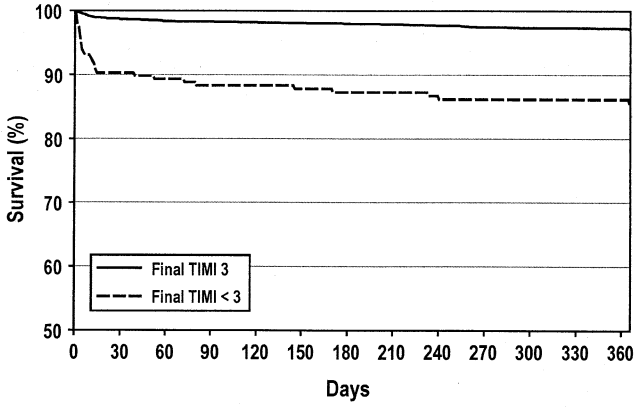

Figure 1. One-year adjusted survival using the Cox proportional hazards model among patients undergoing primary percutaneous coronary intervention with final TIMI <3 flow compared with those with final TIMI 3 flow. $p < 0.0001$ for the difference in adjusted survival.

Clinical and angiographic factors associated with risk of TIMI ≤2 flow in patients undergoing primary PCI. Few previous studies involving a small number of patients have evaluated predictors of TIMI ≤2 in patients with acute STEMI undergoing primary PCI (25–27). These studies have identified the absence of preinfarction angina, higher Killip class at presentation, number of Q waves on presenting electrocardiogram, TIMI 0 flow at initial angiography, anterior myocardial infarction, hyperglycemia, wall motion score on echocardiography, and intravascular ultrasound findings (abnormal lipid pool-like image and lesion elastic membrane cross-sectional area) as predictors of TIMI ≤2

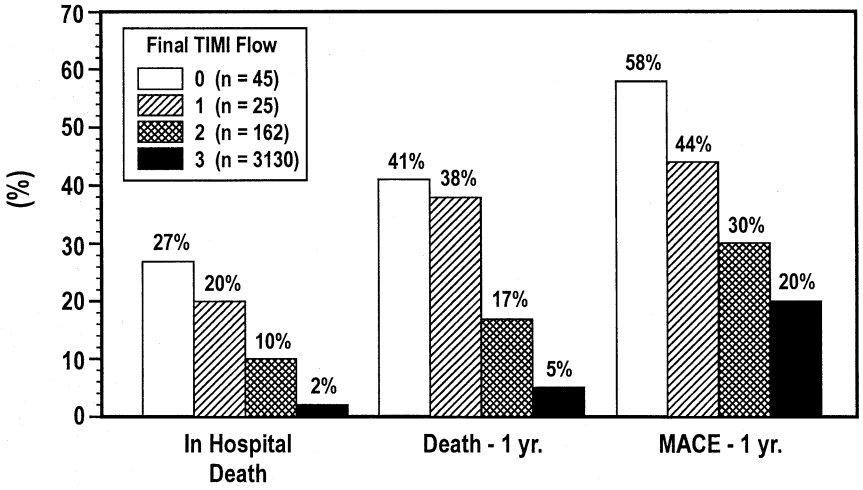

Figure 2. Relationship of final TIMI flow grades after primary percutaneous coronary intervention with in-hospital and one-year mortality and major adverse cardiovascular events (MACE). p for trend <0.0001 for all three outcomes.

flow. In our study, although univariate analysis revealed several clinical and angiographic factors to be associated with TIMI ≤2 flow (Tables 1 and 2), multivariate analysis showed age ≥70 years, diabetes, longer time to emergency room presentation, initial TIMI 0 or 1 flow, and LVEF < 50% to be associated independently with the increased risk of TIMI ≤2 final flow. Final TIMI ≤2 flow is thought to be due to microvascular dysfunction resulting from vasospasm, distal embolization, endothelial dysfunction secondary to endothelial injury, capillary plugging by platelets, neutrophils, and erythrocytes, and intracellular and interstitial edema (28). Older age and diabetes are associated with significant cardiovascular structural and physiologic changes, including increase in coagulation factors (tissue factors VII, VIII, and IX), altered neurohormonal and autonomic influences, and endothelial and vascular smooth muscle dysfunction, all of which may contribute to greater vascular reactivity and tone as well as coagulation and sludge formation in the microvasculature (29–31). The longer delay from symptom onset to the emergency room leads to greater myocardial necrosis, leading to more cellular edema and microvascular injury as well as the development of larger clot burden in the infarct-related vessel that is more likely to cause distal embolization and sludging after primary PCI. Initial patency of artery may suggest lower clot burden, spontaneous lysis of the clot, favorable endogenous thrombolysis, resolution of vasospasm and is associated with smaller infarct size as opposed to patients with initial TIMI ≤1 flow. Low LVEF is generally related to a larger infarct size that, besides causing more microvascular damage and interstitial edema, also decreases the coronary perfusion pressure as a result of higher left ventricular end-diastolic pressure. Thus, these common pathophysiologic mechanisms between the development of no-reflow and STEMI in patients with the risk variables may explain in part the association of these variables with TIMI ≤2 flow.

Table 4. Adjusted Odds Ratios of Clinical Variables Associated With the Risk of Final TIMI ≤2 Flow

Outcome	Odds Ratio	95% Confidence Interval	p Value
Age ≥70 yrs	1.57	1.11–2.20	0.01
Diabetes mellitus	1.85	1.27–2.71	0.002
Onset of chest pain to emergency room arrival (per every hour delay in arrival)	1.11	1.06–1.17	< 0.0001
Initial TIMI ≤1	3.24	1.91–5.51	< 0.0001
LVEF <50%	1.72	1.23–2.42	0.002

Model c-statistic 0.68, Hosmer-Lemeshow chi-square = 11.4, degrees of freedom 8, p = 0.18.
LVEF = left ventricular ejection fraction; TIMI = Thrombolysis In Myocardial Infarction.

Clinical implications. It is clear from previous studies and our findings that TIMI ≤2 flow leads to poor in-hospital and one-year outcomes. Thus, an attempt should be made to achieve not only optimal reduction of stenosis of epicardial coronary arteries but also normal microvascular flow. Of the variables found to be associated with TIMI ≤2 flow in our study, only longer time to emergency room presentation could potentially be modified with increased public education of the symptoms of heart attacks and the importance of seeking immediate medical attention when they occur. Alternatively, newer preemptive strategies that have been shown to reduce the occurrence of final TIMI ≤2 flow may be important adjuncts to primary PCI and should be used in high-risk patients. These strategies include the use of primary stenting (6–9,17,32), distal protection devices (33), thrombectomy with angiojet (34), and the liberal use of adjunctive therapies such as intracoronary adenosine, nitroglycerine, nitroprusside, verapamil, and nicorandil (28) or intravenous abciximab (12,16). The role of facilitated coronary angioplasty in improving final TIMI flow needs to be proved in future studies (35). In addition, limitation of infarct size (particularly by reducing the door-to-balloon time), better management of stenosis, and avoidance of

dissection may all help achieve normal flow after primary PCI. These strategies should be employed liberally in patients with STEMI undergoing primary PCI, particularly those patients having risk factors for developing TIMI ≤2 flow as identified in our study. More research is obviously needed to establish if this approach to patients undergoing primary PCI will reduce the rate of post-procedural suboptimal coronary flow.

The underlying mechanism by which final TIMI ≤2 flow in patients undergoing primary PCI results in adverse outcomes is unclear. Although a direct causal relationship may be possible, it cannot be inferred from this study because of the retrospective nature of our investigation. Alternately, the clustering of final TIMI ≤2 flow in high-risk groups (older age, diabetes, delay to emergency room arrival, lower initial TIMI flow, and lower LVEF) suggests the possibility that TIMI ≤2 flow may be a surrogate marker of these high-risk patient characteristics, explaining the poor prognosis of these patients. Future studies are needed to address these issues.

Conclusions. Our study demonstrates that TIMI ≤2 flow occurs infrequently in patients with STEMI undergoing primary PCI and is associated with a higher incidence of adverse events in the cardiac catheterization laboratory and in-hospital, that persists at one year of follow-up. Furthermore, our study identified contemporary clinical and angiographic factors which are strongly correlated with the risk of TIMI ≤2 flow after primary PCI. Knowledge of these factors may help clinicians identify the high-risk subgroup that may be targeted for management strategies before and during intervention with the intention of reducing the occurrence of TIMI ≤2 flow after primary PCI and ultimately reducing the adverse events that frequently complicate this cohort.

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